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SUTHERLAND ASBILL & BRENNAN LLP
999 PEACHTREE STREET, N.E.
ATLANTA, GA 30309

EXAMINER	
PRIEBE, SCOTT DAVID	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,301	LOSER ET AL.	
	Examiner	Art Unit	
	Scott D. Priebe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2003 and 18 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *9 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 10-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-8, 10-17, in the reply filed 8 Dec. 2003 is acknowledged. The traversal is on the ground(s) that the search of all groups would not be unduly burdensome. This is not found persuasive because the application was filed under 35 USC 371, and the basis for restriction under 35 USC 121 and 372 is dictated by PCT Rules. Burden of search and examination is not at issue under PCT rules concerning lack of unity of invention. Even so, the search for adenoviral vectors based upon an ovine mastadenovirus, a bird adenovirus or a bovine atadenovirus or mastadenovirus is not required in a search for adenoviral vectors based upon an ovine atadenovirus, such as OAV287.

The elected invention is a method for transferring genetic material into cultured cells using an ovine atadenoviral vector. Claim 1 is not limited to delivery to cells in a mammal, but embrace the elected invention of delivery to cultured cells. Claims 9 and 18 recite limitations that are directed to *in vivo* administration, when read in light of the specification (pg. 7, lines 9-22).

The requirement is still deemed proper and is therefore made FINAL.

Claims 9 and 18 entirely, and claims 1-4, 6-8, 10-13, and 15-17, as directed to methods for genetic transfer *in vivo* or *in vitro* using bird adenovirus, ovine mastadenovirus, and bovine atadenovirus and mastadenovirus vectors, and claims 1-9 as directed to methods for genetic transfer *in vivo* using an ovine atadenovirus vector, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable

generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed 8 Dec. 2003.

Specification

The disclosure is objected to because of the following informalities: In the amendment to the specification filed 15 Jul. 2003, the inserted material is in error. The instant application cannot claim priority to the PCT application, since it is the PCT application; "claims priority to" should be replaced with -- is a 371 application of -- or a comparable phrase. Also, the PCT was not filed on "December 3, 2001." It was filed 04 Aug. 2000 and amended on 03 Dec. 2001.

Appropriate correction is required.

Claim Objections

Claims 1-8, 10-13, and 15-17 are objected to because of the following informalities:

Claims 1-8, 10-13, and 15-17 are directed in part to non-elected inventions. The claims should be amended to reflect the election of group I, directed to transfer of genetic material to cultured cells using an ovine atadenovirus vector.

Claims 2, 8, 11 and 17 are not in proper Markush format, --the group consisting of-- should be inserted after "selected from."

Claims 2 and 11 recite "the adenovirus ... is selected from mammals and birds." Mammals and birds are not an adenovirus. It is suggested that "mammals and birds" be replaced with --a mammalian adenovirus and a bird adenovirus--.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 10-17 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Amended claims 1-6 and 10-17 are broadly directed to methods for transfer of a "recombinant genetic material," which comprises DNA of a non-human adenovirus encoding at least a viral coat and one or more DNA sequences heterologous to the adenovirus. Applicant has not indicated where the originally-filed disclosure supports the amendments, as is Applicant's burden. MPEP 714.02, last sentence of the third paragraph from the end and 2163.06 (I) last sentence. The rejected claims contain new matter, which was not described in the original disclosure.

The original claims were directed to the use of non-human adenoviral vectors, which included the "genetic material" of the vector packaged into virions with the coat of the non-human adenovirus. The original specification describes non-human adenoviral vectors and methods of using them to deliver "genetic material," and indicates (page 1, 1st para.) that the invention is related to non-human adenoviral vectors.

In contrast, the amended claims are not limited to methods where non-human adenoviral vector virions are used to transfer the genetic material. The claimed methods embrace any genetic material so long as it contains sequences encoding a coat of non-human adenovirus, and the coat proteins need not be expressed. The claims do not require, either implicitly or explicitly, that the genetic material be packaged in the coat of a non-human adenovirus, or that the adenoviral DNA include sequences required for replication and packaging the genetic material into the non-human adenovirus virion. There is no evidence of record that at the time the application was filed, Applicant had contemplated or was in possession of the invention now being claimed. It is suggested that the claims be amended to clearly indicate, either implicitly or explicitly, that the genetic material is packaged into the virion of the non-human adenovirus, and that the genetic material comprise all non-human adenoviral DNA required for replication and packaging of the genetic material in a cell naturally permissive for replication and packaging of the non-human adenovirus upon which the adenoviral vector is based.

In addition, amended claims 1-9 are directed to transferring genetic material into muscle or tumor cells. The claims are not limited with respect to whether the cells are *in vitro* or *in vivo*. Claims 7 and 8 are specifically directed to transfer into human skeletal muscle, either *in vitro* or *in vivo*. New claims 16 and 17 are specifically directed to transfer of genetic material into cultured human skeletal muscle cells. The original specification (e.g. page 3, lines 31-34; page 6, lines 26-35; page 8, lines 9-30; pages 12-15) describes transfer to tumors and skeletal muscle *in vivo*, but not to cultured tumor or skeletal muscle cells (or cell types found in skeletal muscle). Where the specification discusses transfer to cultured cells or cells *in vitro*, it mentions human cells in general (page 7, line 35 to page 8, line 7) and IMR-90 cells (human lung fibroblast cell

line) and human liver-derived cells specifically (page 7, lines 24-33; page 16). No mention is made of using tumor cells or skeletal muscle cells (or skeletal muscle-derived cells) in culture or *in vitro*. Thus, the original disclosure does not provide support for transfer to tumor cells or human skeletal muscle cells in culture or *in vitro*, as is now claimed. There is no evidence of record that Applicant had contemplated transfer of genetic material to tumor cells or human skeletal muscles cells in culture or *in vitro*, or was in possession of these embodiments.

Claims 1-8 and 10-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for embodiments of the elected invention wherein the genetic material is packaged or encapsidated into an OAV287 coat (capsid) and the non-human adenoviral DNA sequences comprise all DNA sequences of an OAV287 genome required for replication and packaging of the genetic material into the OAV287 capsid in CSL-503 fetal ovine lung cells, does not reasonably provide enablement for any other embodiments of the elected invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are broadly directed to methods for transfer of a "recombinant genetic material," which comprises DNA of a non-human adenovirus encoding at least a viral coat and one or more DNA sequences heterologous to the adenovirus. The claims do not require that the genetic material be a non-human adenoviral vector, be packaged into an non-human adenoviral coat (capsid), or that the non-human adenoviral DNA comprise all sequences required for replication and packaging of the genetic material into the capsid in cells naturally permissive for

replication and packaging of the non-human adenovirus. As indicated above, the breadth of these claims beyond encapsidated adenoviral vectors is new matter. The elected invention is at least directed to adenoviral vectors based upon ovine atadenovirus, e.g. OAV287.

All guidance relating to delivery of "genetic material" is directed to adenoviral vectors based upon non-human adenoviruses, e.g. OAV287. The specification relies entirely on the prior art for the construction of such vectors. i.e. the specification provides no direct guidance on the construction of such vectors. Vectors based upon OAV287 were known in the prior art, e.g. WO 96/03508 and WO 97/06826. These vectors either contain all or nearly all OAV287 adenoviral DNA sequences, and all DNA sequences required for replication and packaging of the vector genome into virions. Such sequences would include those required in *cis*, e.g. ITRs and a packaging sequence, and sequences encoding adenoviral proteins and RNA required for replication and packaging of the genome in its natural host cells, e.g. CSL-503 fetal ovine lung cells. As disclosed in WO 96/03508, the genomic organization and genes of OAV287 are very different from that of mammalian mastadenoviruses, such as human Ad2 and Ad5 (pages 3, 15-17). Both (Immunol. Cell Biol. 82: 189-195, 2004) is a review of the state of the art of ovine atadenovirus vectors before and well after the instant invention was made. It discloses (page 192) that at the time the instant invention was made, only three sites of insertion for foreign DNA into OAV287 were known, and that a substantial amount of work was required to develop OAV287 vectors to reach that point, primarily because the virus was uncharacterized at that time. Both also discloses that OAV287 was known, at the time the invention was made, to replicate efficiently only in CSL-503 cells (replication in HVO156 cells was discovered later). Consequently, prior art knowledge on the construction of mastadenoviral vectors is of little or no

use for construction of vectors based upon OAV287. There is no prior art of record describing the construction of replication-defective OAV287 vectors or complementing cells lines that express OAV287 proteins that would complement deleted OAV287 genes required for replication in cells naturally permissive for replication and packaging of OAV287, e.g. CSL-503 cells. At the time the invention was made, the only OAV287 vectors known were those in which foreign DNA was inserted into what was essentially a complete OAV287, such that the vectors were replication competent in the same cells as wild type OAV287.

Therefore, in view of the breadth of the claims, the lack of guidance on construction of ovine atadenoviral vectors, and the state of the prior art of ovine atadenovirus vectors being limited to those capable of replication and packaging in host cells naturally permissive for OAV287 itself, it would have required undue experimentation by one of skill in the art to develop OAV287 vectors commensurate in scope with the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 8, 16 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7 and 16 recite that the cells are human skeletal muscle cells. Claims 8 and 17 recite that fibroblasts, dendritic cells, endothelial cells are skeletal muscle cells. While fibroblasts, dendritic cells, and endothelial cells may be found in skeletal muscle along with skeletal muscle cells, the former are not muscle cells *per se.* Where applicant acts as his or her

own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). It is suggested that claims 8 and 17 be amended by replacing "a human skeletal muscle cell" with -- a cell from human skeletal muscle--, and claims 8 and 17 be amended by replacing "human muscle cell" with -- cell from human skeletal muscle--.

Also, claims 8 and 17 recite "combinations" of different cells in reference to "the human muscle cell." It is not clear how a single cell can be a combination of cells.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 10-15 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Both, WO 97/06826.

See page 10, line 18, to page 11, line 5.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy J. Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Scott D. Priebe

Scott D. Priebe
Primary Examiner
Art Unit 1632